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Meta-analysis of studies of passive smoking and lung cancer: effects of study type and continent

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Background To calculate a pooled estimate of relative risk (RR) of lung cancer associated with exposure to passive smoking in never smoking women exposed to smoking spouses. This study is an updated meta-analysis that also assesses the differences between estimated risks according to continent and study type using meta-regression.

Methods From a total of 101 primary studies, 55 studies are included in this meta-analysis, of which, 7 are cohort studies, 25 population-based case-control and 23 non-population-based case-control studies. Twenty previously published meta-analyses are also reviewed. Fixed and random effect models and meta-regression are used to obtain pooled estimates of RR and *P*-value functions are used to demonstrate consistency of results.

Results The pooled RR for never-smoking women exposed to passive smoking from spouses is 1.27 (95% CI 1.17–1.37). The RR for North America is 1.15 (95% CI 1.03–1.28), Asia, 1.31 (95% CI 1.16–1.48) and Europe, 1.31 (1.24–1.52). Sequential cumulative meta-analysis shows no trend. There is no strong evidence of publication bias.

Conclusions The abundance of evidence, consistency of finding across continent and study type, dose–response relationship and biological plausibility, overwhelmingly support the existence of a causal relationship between passive smoking and lung cancer.

Keywords passive smoking, lung cancer, meta-analysis

Introduction

Lung cancer has been identified as the most frequently occurring cancer in the world with 1.2 million new cases diagnosed in the year 2000 (12.3% of the world's total cancer incidence).[1] Active tobacco smoking is the major known cause of lung cancer. The influence of tobacco smoke in inducing lung and non-lung cancers is likely to be due to 60 known or suspected carcinogenic chemicals contained in tobacco smoke.[2,3] The harmful effect of active smoking on lung cancer is well documented, and environmental tobacco smoke (ETS) has been classified as a known (Group A) human lung carcinogen by the United States Environmental Protection Agency (EPA) since 1993.[4] Since then, ETS has been the most widely studied risk factor of lung cancer among non-smokers.[5]

Passive smoking contains smoke from two sources: sidestream and exhaled mainstream smoke. At least 17 carcinogenic chemicals contained in tobacco smoke are emitted at higher levels in sidestream smoke than mainstream smoke.[6–8] One of the metabolites of tobacco smoke [benzo (a) pyrene diol epoxide], which shows a direct aetiological association with lung cancer, is found in both mainstream and sidestream smoke.[9] The present knowledge about the carcinogenic activity of sidestream smoke, the lack of any evidence to identify a minimum threshold for tobacco smoke inducing lung cancer and monotonic increase in the risk of lung cancer with increased amount smoked,[2,10,11] suggest that an association between passive smoking and lung cancer is biologically plausible.

Numerous epidemiological studies since 1981 have examined the association between passive smoking and lung cancer. The tobacco industry has criticized the statistical evidence and

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much effort has gone into considering the possible effects of confounding factors and misclassification.

Exposure to ETS by non-smoking spouses of smokers is one of the sources of adult exposure to passive smoking that has been frequently studied because it is less likely to be subject to misclassification or other bias than other exposure scenarios. This meta-analysis is an update of a previous study[12] which includes more recent primary studies and compares pooled estimates from studies classified by continent, study design and year of study using sensitive measures to detect effect differences.

Methods

Primary studies of ETS and lung cancer were identified through a computerized literature search of Medline and Embase (up to December 2006), using appropriate key words [(passive smoking or environmental tobacco smoke) and (lung cancer or lung carcinoma or carcinoma of lung or bronchial carcinoma) and (cohort or case control)]. In addition, all citations in each study were reviewed. Moreover, to capture further articles relevant to the topic, experts in the field of passive smoking were approached. We included all the publications in the peer-reviewed scientific press in the public domain if they examined the relationship between ETS and lung cancer among never-smoking women exposed to spousal smoke compared with never-smoking women exposed to non-smoking spouses.

Studies were classified by type of design (cohort and case-control), and case-control studies were further classified into those with or without population-based controls. If a study had multiple publications, the results were included only once, and the preference was to include the study with the most cases and/or longer follow-up. Adjusted estimates of risk [relative risks (RR) or odds ratios (OR)] or unadjusted estimates (if adjusted results were not available) were extracted for each study. In addition, all published meta-analyses examining the relationship between lung cancer and domestic spousal exposure to ETS were considered in this study. All primary studies included in the meta-analysis were evaluated by two reviewers.

One hundred and one papers published between 1981 and 2006 were identified. Of these studies, we excluded those that reported the same cases or subsets of cases[13–26] and studies in which interaction between genetic background and ETS were examined.[27–29] We also excluded studies in which there was no report on risk among non-smokers alone,[30] or if the article had not specifically stated that all the subjects were never-smokers.[31–40] The articles which reported combined results for males and females were excluded.[24,41–50] Studies by Hole *et al.*,[44] Kubik *et al.*[51] and Katada *et al.*[52] were excluded because the number of never-smoking women were 6, 5 and 2, respectively. The studies by Shen *et al.*,[40] Rachtan[53] and Xu *et al.*[54] were excluded because there were no clear statements to indicate that risks were due to spousal exposure. We also excluded those articles with dead cases and controls, those without formal controls, and those studies with controls that included patients with diseases associated with smoking.[55–57] The study by Garfinkel[58] was replaced with the study by Enstrom and Kabat[59] as the later contains more person-years of follow-up.

Statistical analysis

The data were analysed using Stata version 8.[60] We used inverse-variance weighting to calculate fixed and random effects summary estimates and to produce a forest plot. Where the studies showed no significant heterogeneity, a fixed effects model was used. In addition to the overall pooled RR, results were pooled according to type of study (cohort studies, population-based case-control and non-population-based case-control studies) and continent in which the study was conducted (North America, Europe and Asia). Furthermore, studies were classified as Western (including North America and Europe) and non-Western studies. We plotted the *P*-value function for pooled RR of effect by type of study and continent.[61] Cumulative meta-analysis in which the cumulative results at the time each study was published were calculated and graphed. Publication bias was checked using a modification of Macaskill's test.[62] In addition, to assess the effect of possible publication bias, we calculated the pooled RR adjusted for publication bias using the 'trim and fill' algorithm.[63] Meta-regression was used to analyse association between the pooled RR and study characteristics (study type and continent of study).

Results

A total of 55 studies, seven cohort and 48 case-control studies are included in the meta-analysis. In 45 of these studies (82.0%) there is an increased risk for lung cancer among non-smoking women (RR or OR > 1). In only one study the OR is less than 1.0 with 95% CI excluding unity (OR = 0.70, 95% CI 0.60–0.90) (Tables 1–3).

Risk associated with exposure to passive smoking

Table 4 and Figure 1 show the estimated pooled RR associated with exposure to ETS. The pooled RR from all 55 studies is 1.27 (95% CI 1.17–1.37). Figure 2 shows the *P*-value function for pooled estimates of effect by type of study demonstrating substantially overlapping results, although results from non-population-based case-control studies tend to be somewhat higher.

Stratification of the studies by continent of origin shows that the RR for lung cancer for exposure of never-smoking women to spousal ETS is 1.31 for studies conducted in Europe (95% CI 1.24–1.52) compared with 1.15 (95% CI 1.03–1.28) for North America and 1.31 (95% CI 1.16–1.48) for studies conducted in Asia (Table 4). The corresponding RR in studies of Western countries is 1.20 (1.10–1.31). Figure 3 and results of meta-regression in Table 4 show the lack of regional differences.

Cumulative relative risk and publication bias

Figure 4 shows the pooled cumulative RR from 1981 to 2006 with no evident trend. Using a modification of Macaskill's test, there is no evidence of publication bias among 48 studies in which there are available data about the sample size (*P*-value for bias = 0.80). As the lack of evidence of bias could be due to inadequate statistical power we used a non-parametric method of 'trim and fill' and estimated 13 possible missing studies. The estimated RR for 68 studies, including the 'missing' studies,

Table 1 Relative risks for lung cancer in studies of never-smoking females exposed to spousal smoking, 1981–2006, cohort studies ($n = 5$)

Authors	Country	Unadjusted RR	95% CIs*	Adjusted RR	95% CIs*
Hirayama[14,15,65,144]	Japan	1.38	0.97–1.98	1.45	1.02–2.08
Cardenas *et al.*[66]	US	1.2	–	1.2	0.8–1.6
Jee *et al.*[79]	Korea	2.0	1.10–3.80	1.90	1.0–3.50
Speizer *et al.*[160]	US			1.5	0.3–6.3
Nishino *et al.*[145]	Japan	1.5	0.57–4.2	1.8	0.67–4.6
Garfinkel [58]; Enstrom and Kabat[59]	US	0.99	0.72–1.37	0.94	0.66–1.33
Wen *et al.*[161]	China			1.09	0.74–1.61
Pooled RR (Fixed effects)		RR = 1.22;	95% CI = 1.03–1.44		

*95% Cis, 95% confidence intervals.

Table 2 Odds ratios for lung cancer in studies of never-smoking females exposed to spousal smoking, 1981–2006

Authors	Country	Unadjusted OR	95% CIs*	Adjusted OR	95% CIs*
Koo *et al.*[17,87]	Hong Kong	1.55	0.90–2.67	1.64	0.87–3.09
Buffler *et al.*[88]	US	0.81	0.34–1.90	–	–
Wu *et al.*[85]	US	1.41	0.54–3.68	1.20	0.60–2.50
Akiba *et al.*[68]	Japan	1.52	0.88–2.63	1.50	0.87–2.59
Gao *et al.*[69]	China	1.19	0.82–1.73	1.30	0.87–1.94
Humble *et al.*[70]	US	2.34	0.81–6.75	2.20	0.75–6.47
Lam *et al.*[71]	Hong Kong	1.65	1.16–2.35	–	–
Pershagen *et al.*[72]	Sweden	1.28	0.76–2.16	1.20	0.70–2.10
Svensson *et al.*[119]	Sweden	1.26	0.57–2.81	1.4	–
Wu-Williams *et al.*[64]	China	0.79	0.62–1.02	0.70	0.60–0.90
Fontham *et al.*[19,20]	US	1.26	1.04–1.54	1.29	1.04–1.60
Liu *et al.*[146]	China	0.74	0.32–1.69	0.77	0.30–1.96
Brownson *et al.*[82]	US	1.00	0.80–1.20	–	–
Stockwell *et al.*[80]	US	–	–	1.60	0.80–3.00
De Waard *et al.*[147]	Netherlands	2.57	0.83–7.85	–	–
Du *et al.*[21], Lei *et al.*[93]	China	1.19	0.66–2.16	–	–
Sun *et al.*[148]	China	–	–	1.16	0.80–1.69
Zheng *et al.*[78]	China	2.52	1.03–6.44	–	–
Zhong *et al.*[94]	China	–	–	1.1	0.8–1.5
Boffeta *et al.*[149]	Europe			1.0	0.5–1.9
Wang *et al.*[84]	China	–	–	1.15	0.6–2.1
Johnson *et al.*[83]	Canada	–	–	1.2	0.5–2.8
Kreuzer *et al.*[150]	Germany	–	–	1.67	0.86–3.25
McGhee *et al.*[162]	Hong Kong			1.38	0.94–2.04
Yu *et al.*[163]	China			1.35	0.69–2.62
Pooled OR (Fixed effects)		OR = 1.18;	95% CI = 1.08–1.28		

*95% CIs: 95% confidence intervals.
Case control studies with population-based controls ($n = 23$).

is not substantially different from our estimate without adjustment for missing studies: RR = 1.17 (95% CI 1.08–1.25).

Heterogeneity between studies

There is some evidence suggestive of heterogeneity between the 55 studies ($\chi^2 = 67.6$; df = 54; $P = 0.04$) and therefore a random effect model is used to estimate the pooled effect (Table 4). Further examination of studies shows that the source of heterogeneity is among the 28 studies carried out in Asia ($\chi^2 = 43.7$; df = 27; $P = 0.02$). To examine the effect of the heterogeneity between studies of continent and type of study in more detail, a pooled RR is estimated using meta-regression. None of these factors has a substantial effect on the results (Table 4). The only source of heterogeneity is the study by Wu-Williams *et al.*[64] which shows an implausible protective

Table 3 Odds ratios for lung cancer in studies of never-smoking females exposed to spousal smoking, 1981–2006

Authors	Country	Unadjusted OR	95% CIs*	Adjusted OR	95% CIs*
Trichopoulos *et al.*[16,151]	Greece	2.08	1.20–3.59	–	–
Chan & Fung [152]	Hong Kong	0.75	0.43–1.30	–	–
Correa *et al.*[73]	US	2.07	0.81–5.25	–	–
Kabat and Wynder [117]	US	0.79	0.25–2.45	–	–
Garfinkel *et al.*[89]	US	1.31	0.87–1.97	1.23	0.81–1.87
Lee *et al.*[90]	UK	1.03	0.41–2.55	1.00	0.37–2.71
Brownson *et al.*[153]	US	1.82	0.45–7.36	1.68	0.39–6.90
Geng *et al.*[67]	China	2.16	1.08–4.29	–	–
Inoue and Hirayama [74]	Japan	2.55	0.74–8.78	2.54	0.80–8.80
Shimizu *et al.*[118]	Japan	1.08	0.64–1.82	–	–
Kalandidi *et al.*[86]	Greece	1.62	0.90–2.91	1.92	1.02–3.59
Sobue *et al.*[154]	Japan	1.06	0.74–1.52	1.13	0.78–1.63
Liu *et al.*[75]	China	1.66	0.68–4.11	–	–
Kabat *et al.*[91]	US	1.08	0.60–1.94	–	–
Wang *et al.*[155]	China	2.5	1.3–5.1	–	–
Wang *et al.*[76]	China	–	–	1.11	0.65–1.88
Jokel *et al.*[22], Nyberg *et al.*[23] and Boffetta *et al.*[77]	Europe	–	–	1.11	0.88–1.39
Zaridze *et al.*[156]	Russia	–	–	1.53	1.06–2.21
Rapiti *et al.*[92]	India	–	–	1.2	0.50–2.90
Lee *et al.*[81]	Taiwan	–	–	2.2	1.5–3.3
Seow *et al.*[157]	Singapore	1.3	0.9–1.8		
Zatloukal *et al.*[158]	Prague	–	–	0.66	0.22–1.96
Gorlova *et al.*[164]				1.29	0.65–2.57
Pooled OR (Fixed effects)		OR = 1.33;	95% CI = 1.19–1.48		

*95% Cis, 95% confidence intervals.
Case control studies with non-population-based controls ($n = 22$).

Table 4 Meta-analysis of studies by type of study and continent, 1981–2006

Studies	Number	Pooled estimate	95% CI	*P*	Test for heterogeneity	Model	Ratio of relative risk[a]	95% CI
Type of study								
Cohort	7	1.22	1.03–1.44	$P = 0.021$	$P = 0.43$	Fixed	1.00[b]	
Case-control population-based	25	1.18	1.08–1.28	$P < 0.001$	$P = 0.23$	Fixed	0.97	0.76–1.23
Case-control non-population-based	23	1.33	1.19–1.48	$P < 0.001$	$P = 0.12$	Fixed	1.06	0.81–1.37
Continent								
North America	16	1.15	1.03–1.28	$P = 0.013$	$P = 0.83$	Fixed	1.00[b]	
Europe	11	1.31	1.24–1.52	$P = 0.001$	$P = 0.31$	Fixed	1.13	0.87–1.46
Asia	28	1.31	1.16–1.48	$P < 0.001$	$P = 0.04$	Random	1.11	0.91–1.33
Total	55	1.27	1.17–1.37	$P < 0.001$	$P = 0.04$	Random		

[a]Values are the results from meta-regression of pooled RR against type of study and continent.
[b]Reference group.

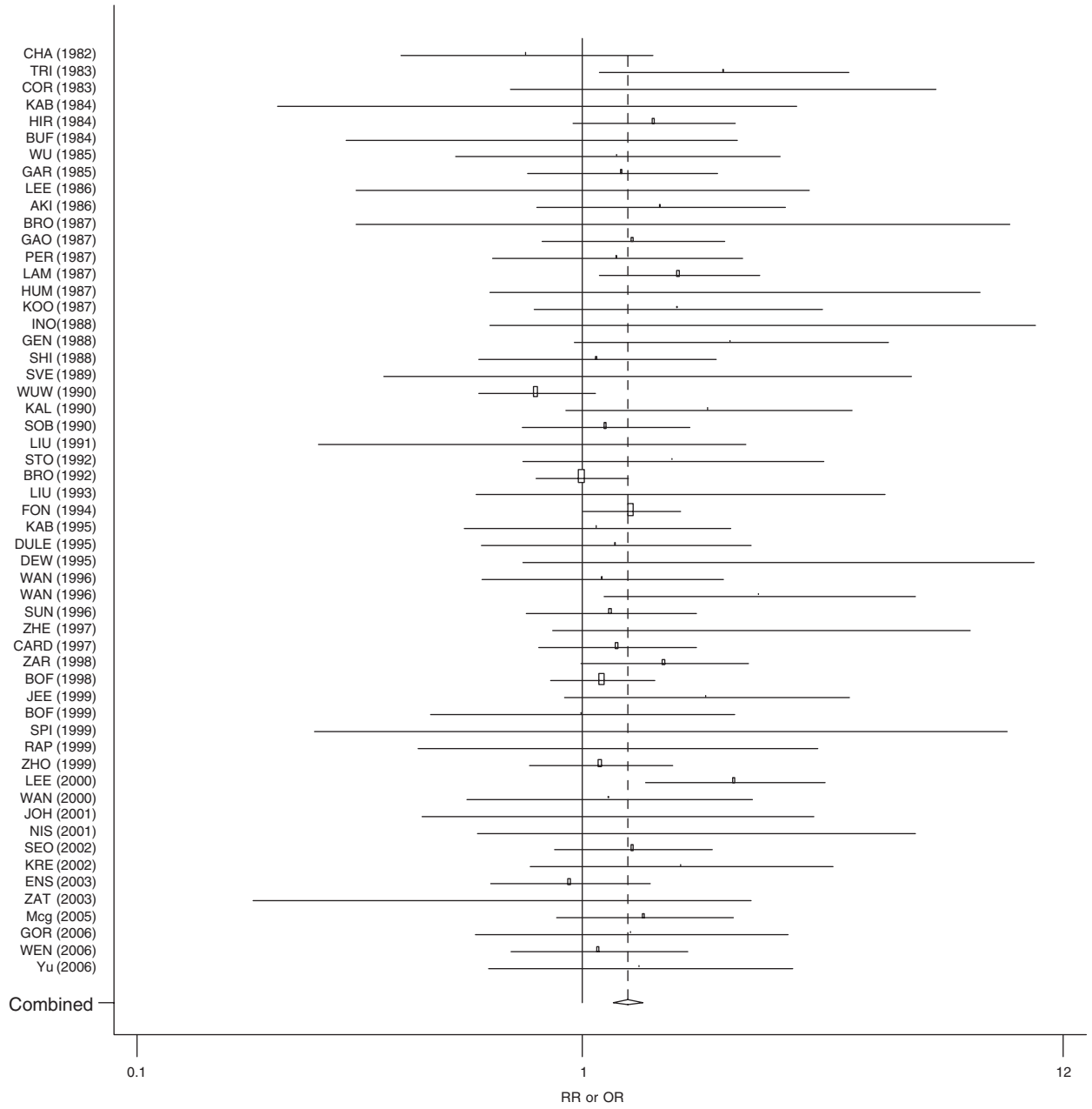

Figure 1 Forest plot of odds ratios and relative risks of lung cancer (and 95% CI) from studies of never smoking women exposed to smoking spouses, 1981–2006

effect of passive smoking on risk of lung cancer (RR = 0.70; 95% CI 0.60–0.90). Exclusion of this study does not change the point estimate of the pooled RR of 1.27 (95% CI 1.17–1.37).

Dose–response relationship

Data on the dose–response relationship between passive smoking and lung cancer are available for 36 studies. Measurement of the passive smoking 'dose' is recorded in one of three ways: cigarettes per day; years of living with a husband who smoked or a combined measure of number of cigarettes and years of exposure. Of these 36 studies, 20 demonstrate a dose–response relationship with 95% CI excluding unity for one or all of the ETS 'dose' measures.[16,20,65–81] Five studies show a positive dose–response association but the 95% CIs include unity,[82–86] and in 11 studies there is no evidence of a dose–response relationship.[40,59,87–94]

Other meta-analyses

There are 23 published meta-analyses examining the relationship between exposure to ETS and lung cancer. Twenty of the meta-analyses combined only spousal studies (Table 5),[7,12,95–112] three combined workplace studies,[112–114] and one did not specify the context of the ETS exposure.[115]

The pooled relative risks of the previously published spousal meta-analyses range from 0.91 to 1.44. With the exception of

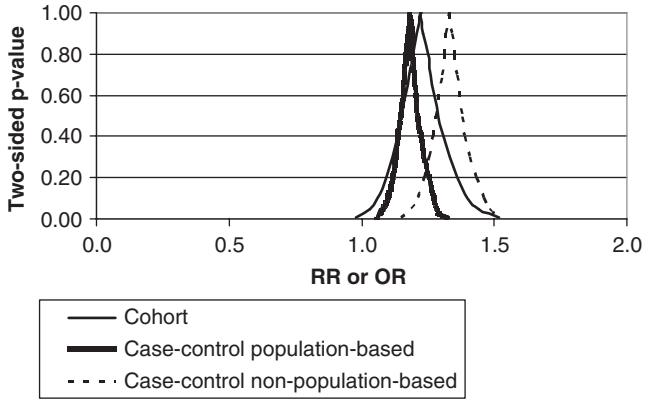

Figure 2 *P*-value functions for pooled odds ratios and relative risks of lung cancer from studies of never smoking women exposed to smoking spouses, by study type, 1981–2006

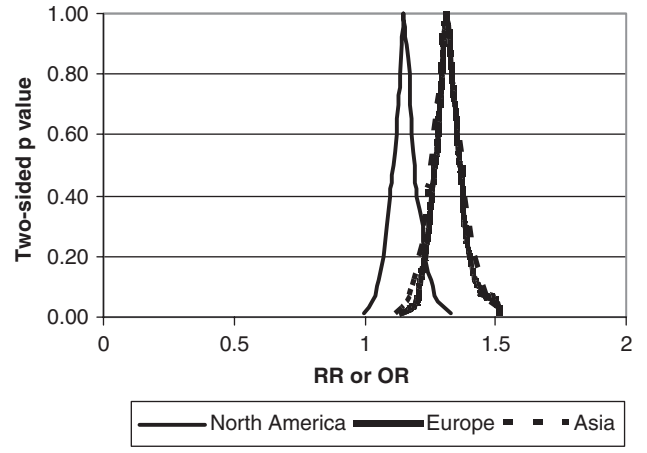

Figure 3 *P*-value function for pooled odds ratios and relative risks of lung cancer from studies of never smoking women exposed to smoking spouses, by continent, 1981–2006

the meta-analysis by Wang and Zhou of six Chinese studies (RR = 0.91; 95% CI 0.75–1.10),[109] these meta-analyses all give estimates with confidence limits that exceed unity. Meta-analyses of studies of exposure to ETS in the workplace yield RR of 1.01 (95% CI 0.92–1.11)[113], 1.39 (95% CI 1.15–1.68)[114] and 1.17 (1.04–1.32)[112]; the second was meta-analysis of five studies meeting basic quality criteria. The meta-analysis which did not specify the context of ETS exposure combined data from three Chinese studies and produced RR = 1.00 (95% CI 0.74–1.35).[115]

Discussion

Using recently published articles, the present meta-analysis shows a 27% excess in risk of lung cancer among never-smoking women exposed to spousal ETS compared with never-smoking women not exposed to spousal ETS. This study supports the results of previous findings from other meta-analyses in showing a positive relationship between passive smoking and lung cancer. In most individual studies and meta-analyses the estimated (or pooled) RR is between 1.2 and 1.4, a level where the possibility of confounding and different types of bias should be carefully explored. By restricting the data to exposure to ETS among never-smoking women, we have minimized some of the difficulties of previous meta-analyses especially in relation to misclassification bias. We have also considered other types of bias and confounding.

Careful analysis of the effect of different study types and studies conducted in different continents indicates that real heterogeneity between the included studies is implausible (Table 4, Figures 2 and 3). This result is consistent with the previous reports showing no evidence of differences between RR of passive smoking on lung cancer by continents and type of study.[95,112]

Our findings are also consistent with results from exposure to ETS in workplace in both men and women.[20,45,77,82,85,86,89–92,116–121] In addition, our results are compatible with the result of those studies using a dosimetric extrapolation of effect of active smoking on lung cancer. For example Puntoni *et al*.[122] concluded that passive smoking can be related with a 17–35% excess risk of lung cancer among never-smokers. Data concerning individuals at the 95th centile of exposure to passive smoking yield a risk much higher than the estimated effects which are based on the average exposure which provide additional evidence of a dose–response relationship.[123]

While smoking is the main risk factor of lung cancer among smokers, several weak risk factors may contribute to the occurrence of lung cancer in never-smokers. Therefore, it could be expected that the final estimated risk may be confounded by various factors. Indeed, a household in which one spouse is a smoker may differ in some aspects from those in which neither is a smoker. Indoor air pollution and lifestyle (such as diet) are two important features in which smoking and non-smoking households may differ. For example, it has been documented that non-smokers living with smokers have a lower intake of micronutrients,[124,125] cholesterol and beta carotene.[126,127] Despite findings published by Lee *et al*.,[128] it has been estimated that the confounding effect of these dietary variables is modest.[18,20,77,86,110,126,129,130]

A possible source of misclassification is uncertainty about personal smoking status. At least part of this misclassification is likely to be systematic as some smokers will deny smoking. Since smokers are likely to marry smokers, therefore, self-reported never-smokers are more likely to actually be ex-smokers or current smokers if married to smokers than self-reported never-smokers married to never-smokers.[102,131,132] It is estimated that such misreporting among females ranges from 1.3 to 3.6% compared with 11.5% among males.[124,133,134] In a meta-analysis by Hackshaw *et al*.,[110] even taking into account of all determinants of misclassification of ever smokers as never smokers[98]—the proportion of ever smokers misreported as never smokers, the estimated risk of lung cancer among misclassified persons, aggregation of smokers and the prevalence of smoking in the population—the estimated risk of lung cancer associated with passive smoking only reduced from 1.24 to 1.18.

Deficiencies in the accurate measurement and reporting of ETS are other factors which may induce misclassification.

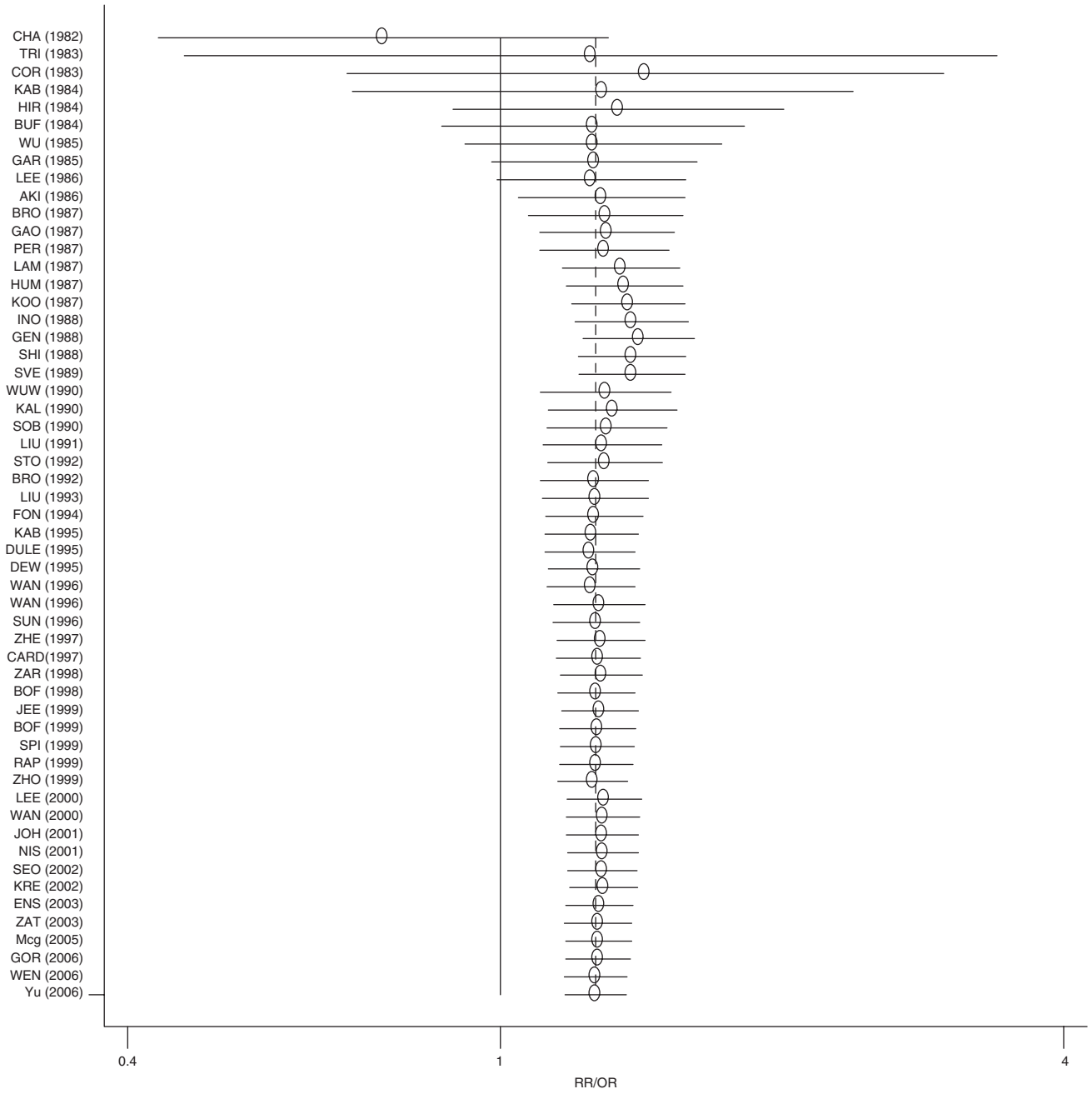

Figure 4 Cumulative meta-analysis of 51 studies of never smoking women exposed to smoking spouses, 1981–2006

As there is no reliable biological marker for ETS exposure, many epidemiological studies rely on questionnaire assessment. For the 25–50% of women who work outside the home, exposure to spousal smoking would be an underestimation of true overall exposure to ETS,[135] since they may also be exposed to ETS in the workplace. Control groups are also subject to misclassification. In fact non-smokers living with non-smokers may be exposed to ETS from workplace and public environment. While the misclassification from inaccurate self-designation as a never smoker would lead to over-estimation of the true risk of lung cancer associated with passive smoking, the additional exposure of controls would underestimate the effect.

Another source of misclassification which would lead to underestimation of the RR is misdiagnosis of lung cancer. In fact there is little evidence of association between passive smoking and cancers other than lung cancer. Misdiagnosis of other forms of cancers with spread to the lung as primary lung cancer, and inclusion of such cases, could induce some systematic bias towards the null. Although new methods for diagnosis of lung cancer (cytological examination) have reduced the possibility for misdiagnosis of this condition,

Table 5 Meta-analyses of spousal studies of passive smoking and lung cancer, 1981–2006

Author	Studies in meta-analysis	Sex(es)	Pooled odds ratios (95% CI)
Blot and Fraumeni[96]	12	F	1.30 (1.10–1.50)
US National Research Council[97]	13	F	1.32 (1.16–1.52)
Wald *et al.*[98]	13	F and M	1.35 (1.19–1.54)
Wells[159]	17	F	1.44 (1.26–1.66)
Saracci and Riboli[100]	14	F and M	1.35 (1.20–1.53)
Lee[101]	28	F	1.18 (1.07–1.30)
Tweedie and Mengersen[102]	26	F	1.17 (1.06–1.28)
US Environmental Protection Agency[7]	11	F	1.19 (1.01–1.39)
Pershagen[103]	25	F	1.23 (1.11–1.36)
Gross[104]	32	F	1.18 (1.06–1.28)
Mengersen *et al.*[105]	34	F	1.23 (1.08–1.41)
Dockery[106]	33	F	1.27 (1.18–1.38)
Law and Hackshaw[107]	34	F and M	1.24 (1.11–1.38)
Tweedie *et al.*[108]	36	F	1.23(1.08–1.39)
Wang[109]	6	F	0.91 (0.75–1.10)
Hackshaw *et al.*[110]	37	F and M	1.26 (1.08–1.49)
Merletti *et al.*[111]	39	F and M	1.24 (1.15–1.34)
Zhong *et al.*[95]	40	F	1.20 (1.12–1.29)
Taylor *et al.*[12]	43	F	1.29 (1.17–1.43)
Boffetta[112]	51	F and M	1.25 (1.15–1.37)
Present study	55	F	1.27 (1.17–1.37)

diagnosis between a primary and secondary lung cancer is still challenging.[112]

This study was restricted to published papers in scientific peer reviewed journals and therefore publication bias has to be considered. Studies with a statistically significant effect are more likely to be published[136] and to be published in English,[137] more likely to be cited by other authors[138] and more likely to have multiple publications.[139] In addition, those articles that show no association between passive smoking and lung cancer may not indicate this in the title or abstract whether passive smoking was assessed (authors' publication bias). The study by Wu-Williams *et al.*[64] is one of these studies. However, publication bias is unlikely to explain the observed excess in risk of lung cancer associated with passive smoking. Cumulative RRs estimated in Figure 4 support this conclusion as the pooled RR has remained almost stable over time. In addition, there is some evidence to show that only a small number of studies of ETS and lung cancer are unpublished.[140] In our study, adjustment for publication bias has little effect on the pooled estimated RR. This finding is consistent with the result of recently published re-analysis of 37 studies by Takagi *et al.*,[141] which yielded an estimate adjusted for publication bias (RR = 1.19, 95% CI 1.08–1.31).

Except for specificity, the association between passive smoking and lung cancer fulfils all other criteria for causation outlined by Bradford Hill.[142] The strength of association (even after consideration of bias and confounding), consistency of findings across domestic and workplace primary studies, dose-response relationship and dosimetric extrapolations and biological plausibility are important criteria which indicate a causal relationship between passive smoking and lung cancer. Furthermore, the evidence is coherent.

Although the excess risk from exposure to passive smoking is small, the high prevalence of exposure to passive smoking in workplaces, restaurants and other public areas in some countries, as well as at home and in private automobiles, make it an important risk factor for lung cancer among non-smoking people.

The tobacco industry tends to understate the effect of passive smoking on occurrence of lung cancer, and has tried to introduce ventilation as a solution for passive smoking in enclosed public areas.[143] But this does not prevent exposure of workers in these areas to passive smoking. The preferable public health policy is still a total ban on smoking in public areas.

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KEY MESSAGES

- The pooled relative risk for exposure to passive smoking from spouses among never-smoked women is 1.27 (95% CI 1.17–1.37).
- The stratified analysis using meta-regression showed no signs of important heterogeneity between case-control and cohort studies or between studies conducted in Europe, Asia and North America.
- Although various confounding factors and biases have some distorting effect on the excess in risk of lung cancer among people exposed to passive smoking, the abundance of evidence, consistency of finding across continent and study type, biological plausibility and dose–response relationship, support the existence of a causal relationship between exposure to passive smoking and lung cancer.

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